

1 Analysis

Through weekly meetings, the Neuroscience Working Group identified *Neural Injury and Repair* as a Signature area. We performed a detailed analysis of grant funding and publications and compared our strength areas to other institutions regionally and within the Big Ten. We identified those areas where we can be “best in class” using three criteria; numbers of Rutgers publications, numbers of Rutgers grants and level of support, numbers of funded Rutgers faculty.

Initially the working group identified three broad research areas in diseases of the developing brain and mature brain and in CNS injury and identified individuals at RBHS and across Rutgers who fit into one or more of these areas:

- 1) **Degeneration, Dysfunction and Aging**, such as occurs in Alzheimer’s disease (AD), Parkinson’s disease (PD), and Multiple Sclerosis (MS).
- 2) **Loss of neural function after injury**, such as occurs in Traumatic Brain Injury (TBI), Spinal Cord Injury (SCI) and Stroke.
- 3) **Loss of neural function during development**, such as occurs in Autism, Schizophrenia, and perinatal hypoxia-ischemia.

(Note: disorders involving post-traumatic stress, anxiety or addictions were not analyzed in detail, as they were the focus of other assigned working groups).

Neurodegeneration, Dysfunction and Aging

Analysis of publications from Rutgers faculty over the past five years in *Neurodegeneration, Dysfunction and Aging* revealed 101 papers related to AD, 130 papers related to PD, and 90 papers related to MS (Table 1). We identified 98 currently funded or recently closed grants in this area: 11 grants on PD (est. \$6.4 mil) and 24 on MS (est.

Table 1: Neuroscience Sub-Area	# Pubs (5 yrs)	PubMed Search Terms
Alzheimer’s Disease	101	Alzheimer*, amyloid, tau, dementia
Parkinson’s Disease	130	Parkinson*, synuclein, dopamine, nigro-striatal
Multiple Sclerosis	90	“Multiple Sclerosis”, oligodendrocyte*
Spinal Cord Injury	77	“spinal cord”
Traumatic Brain Injury	45	“brain injury”
Stroke	113	stroke
Autism	37	autism
Schizophrenia	54	Schizophrenia

\$10.1 mil) (Table 2). Three grants were directly related to AD, however, additional investigators are studying processes related to CNS degeneration and aging (19 PIs; 28 grants) or adult brain function (19 PIs; 32 grants). Several clinical trials were identified in MS and PD. Two endowed chairs exist in MS and one in PD.

Loss of Neural Function after Injury

Analysis of publications from Rutgers faculty over the past five years in *Loss of Neural Function after Injury* revealed 77 papers in SCI, 45 in brain injury and 113 in Stroke. We identified 85 currently funded or recently closed grants in this area: 50 directly related to SCI (est. \$18.1 mil) and 16 related to TBI (est. \$12.3 mil). No grants were identified specifically focused on adult stroke. The remainder of the grants encompassed more general themes within strategies to promote regeneration (8 PIs; 19 grants). The State of New Jersey has supported a number of the grants on both SCI and TBI including two program project grants on TBI, supporting our selection of these areas as areas of excellence. Several clinical trials and private donations were identified in SCI.

Table 2: Neuroscience Sub-Area	# NIH Grants	# Non-NIH Grants	Total \$	# PIs
Alzheimer’s Disease	3	0	\$1,573,040	3
Parkinson’s Disease	6	5	\$6,377,568	9
Multiple Sclerosis	10	14	\$10,154,760	12
Spinal Cord Injury	5	45	\$18,198,287	24
Brain Injury	5	11	\$12,339,911	9
Autism	2	13	\$10,487,672	9
Schizophrenia	3	4	\$5,471,899	4

Table 2. Grant and PI numbers for each category were obtained from internally provided data on RU and RBHS (current and closed grants) and legacy UMDNJ grants for the past 5 years. Multi-year grants were only counted once. All dollar amounts for NIH grants were confirmed on NIH RePORTER and include multi-year funding amounts. Dollar amounts for non-NIH grants could not be independently validated and likely underestimate actual dollars since some were listed as single year amounts.

Loss of Neural Function during Development

Analysis of publications from Rutgers faculty over the past five years in *Loss of Neural Function during Development* revealed 37 papers in the area of Autism and 54 papers in Schizophrenia. We identified 41 currently funded or recently closed grants associated with this sub-area: 15 grants directly related to autism (est. \$10.5 mil) and 7 grants (est. \$5.4 mil) directly related to Schizophrenia. Additional investigators are studying processes related to developmental disorders or injury (15 PIs; 19 grants). New Jersey also supports grants in Autism, including one program project grant, indicating their endorsement of this area.

Based on these analyses, we identified significant current strengths in MS and PD in *Degeneration, Dysfunction and Aging* and in SCI and TBI in *Loss of Neural Function after Injury*. From feedback received on the Interim Report submitted by our working group and from communications with other working groups interested in incorporating Autism and Schizophrenia into their proposals, we focused our Signature Area on *Neural Injury and Repair* to incorporate our strengths in the Neurodegenerative diseases (MS and PD) and Traumatic CNS Injuries (SCI and TBI). We then compared our publications in these strength areas against peer institutions in New York, Connecticut, Philadelphia and New Jersey as well as institutions in the Big Ten to determine Rutgers's ranking in number of publications (Tables 3-6).

In the area of PD, Rutgers ranked 5th in publications regionally and 4th in the Big Ten. An analysis of MS-related publications revealed that we already are "first in class" both regionally and in comparison to the Big Ten. In SCI, we ranked 4th regionally and 6th in the Big Ten in publications. An analysis of publications associated with TBI revealed that we are 5th both regionally and in the Big Ten. SCI and TBI are particularly attractive because the state of New Jersey supports Commissions on Spinal Cord Injury (NJCSCR) and Brain Injury (NJCBI) that have provided significant grant funds to many of our faculty.

Table 3: Parkinson*, synuclein, dopamine, nigro-striatal (# Pubs; 5 yrs)

Regional	Big Ten
Columbia U (301)	U Mich (196)
U Penn (245)	U Minnesota (136)
Yale (218)	Northwestern (134)
Cornell (146)	Rutgers (130)
Rutgers (130)	Indiana (110)
NYU (104)	Purdue (90)
U Rochester (75)	Wisconsin (83)
U Connecticut (55)	U Iowa (72)
Princeton (30)	U Nebraska (70)
	Penn State (67)
	Ohio State (64)
	U Illinois (60)
	MSU (45)

Table 4: "Multiple Sclerosis", oligodendrocyte* (# Pubs; 5 yrs)

Regional	Big Ten
Rutgers (90)	Rutgers (90)
U Penn (64)	Ohio State (70)
Yale (57)	Northwestern (68)
U Rochester (45)	U Wisconsin (47)
U Connecticut (43)	U Illinois (45)
Cornell (37)	U Mich (38)
NYU (35)	Indiana (24)
Columbia U (33)	U Nebraska (23)
Princeton (9)	Penn State (21)
	U Minnesota (17)
	U Iowa (14)
	Purdue (13)
	MSU (8)

Based on our strengths, as well as the relative weaknesses of others in our class, Neurodegenerative Disease (PD and MS) and Traumatic CNS Injury emerge as focus areas where we can develop to be "best in class", both in the New York/ Philadelphia arena and in the Big Ten.

Current Status of Neural Injury and Repair Foci Within Rutgers

The choice of Neurodegenerative Diseases (MS and PD) and Traumatic CNS Injury as our two focus areas is supported by the importance of these conditions for further study. Moreover, the facilities currently available position us to expand these efforts to become "best in class".

Neurodegenerative Diseases

Multiple Sclerosis: There are at least 10,000 patients affected with MS

in the State of New Jersey. Five National Multiple Sclerosis Society (NMSS) recognized centers care for the majority of these patients. Two of these centers with comprehensive status are part of RBHS: The NJ Medical School MS Diagnosis and Treatment Center on the Newark campus, and the Robert Wood Johnson Center for MS on the New Brunswick campus. These Centers offer comprehensive clinical care, basic research in MS,

Table 5: "Spinal Cord" (# Pubs; 5 yrs)

Regional	Big Ten
U Penn (110)	Northwestern (135)
Cornell (88)	U Mich (131)
Columbia U (78)	U Wisconsin (115)
Rutgers (77)	Ohio State (111)
Yale (72)	Indiana (81)
U Rochester (36)	Rutgers (77)
NYU (35)	U Iowa (60)
U Connecticut (10)	U Minnesota (44)
Princeton (5)	Purdue (44)
	U Illinois (39)
	MSU (23)
	U Nebraska (17)
	Penn State (13)

Table 6: "Brain Injury" (# Pubs; 5 yrs)

Regional	Big Ten
U Penn (153)	U Mich (85)
Columbia U (74)	Indiana (61)
Cornell (52)	Ohio State (54)
Yale (48)	Northwestern (48)
Rutgers (45)	Rutgers (45)
U Rochester (42)	U Minnesota (30)
NYU (39)	U Illinois (26)
U Connecticut (20)	Penn State (26)
Princeton (6)	U Wisconsin (24)
	U Iowa (23)
	U Nebraska (22)
	MSU (22)
	Purdue (11)

clinical trials, and post graduate education and are enhanced by close collaboration with basic MS researchers associated with NJMS and RWJMS. These RBHS investigators have established records in obtaining peer reviewed funding from the NIH, the NMSS, and pharmaceutical industry and have contributed significantly to the understanding of the role of glial-neuronal interactions, neurotrophins and immune molecules underlying the immunopathology of MS. Investigators also have contributed to the development of therapies, and identification of biomarkers of treatment response. Several clinical and research post-doctoral fellows were trained at the Rutgers MS Centers. Both Centers have close ties with the other MS Centers in NJ (St. Barnabas, Freehold, Holy Name, and SOM). Increased collaborative opportunities and multi-investigator grants will enhance the research in both clinical and basic science associated with the groups on each campus. Moreover, training grants are necessary to educate the next generation of investigators dedicated to MS research.

Parkinson's Disease: PD and the related progressive supranuclear palsy (PSP), result in considerable morbidity and mortality in the United States each year. More than 3000 patient visits occur annually at the Advanced Parkinson's Disease Center at RWJMS that is recognized by the American Parkinson's Disease Association (APDA) as a Center of Excellence. This Center is the largest in the State of NJ and is staffed by seven internationally recognized faculty members funded by the Michael J. Fox Foundation and industry. The Center offers comprehensive care to patients with PD including a deep brain stimulation (DBS) neurosurgical option. While the center trains several post-doctoral fellows in basic research each year, it lacks the resources to train clinical fellows in Movement Disorders. Moreover, it is focused at RWJMS, and can be benefited by interactions with basic and clinical investigators of the greater Rutgers community

Fundamental past discoveries at this Center focused on elucidation of the genetics and abnormal molecular and cellular events underlying PD and PSP. The Center has proven expertise to discover new compounds and technologically advanced treatment approaches, test them in animal models of human diseases and translate them to clinical trials for patients. The molecule-to-clinic range of the work in PD and PSP that already exists at RWJMS is a model for translational research. An example is the recent launching of the pharmaceutical start-up company Mentinova, Inc. to develop new therapies for PD treatment-related complications. The Center also serves to train the next generation of scientists who come from the USA and around the world.

In addition to the Center at RWJMS, there is a newly established Neurology-Neurological Surgery movement disorders program at NJMS which provides comprehensive diagnostic and therapeutic services, including deep brain stimulation. There are also several basic research laboratories at NJMS whose research focuses on PD. The presence of both basic research and clinical services in PD provide an opportunity for cross campus collaborations for both patient services and research funding.

Traumatic CNS Injury

It is estimated that 12,000 to 15,000 NJ residents suffer brain injuries from traumatic events each year, of which 1000 are fatal. Approximately 175,000 New Jersey residents currently live with disabilities from TBIs. The leading causes of TBI are motor vehicle crashes, falls, assaults, and self-inflicted injuries. A majority of TBIs affect a segment of the population under 35 years of age. Approximately 6,000 NJ residents suffer damage to the spinal cord each year. Efforts in the basic research underlying SCI and TBI have been funded by the NJCSCR and the NJCBIR and have been underway for some years in RBHS and at the greater Rutgers community. However, only a subset of these efforts have resulted in NIH funded grants, a deficiency that we will rectify, moving us to "best in class".

Although there are multiple basic science grants, clinically, there are only 2 NJCBIR and no NJCSCR or NIH funded grants that deal with the prevention or the pathophysiology and treatment of acute and subacute TBI or SCI. University Hospitals affiliated with both NJMS and RWJMS are level 1 trauma centers. However, active programs in these areas of clinical research are not extensive. This, in spite of the fact that University Hospital (Newark) is a level 1 Trauma Center affiliated with NJMS that already has an established Neurotrauma program which is the largest and busiest in the entire New York metropolitan, NJ, Philadelphia areas. It evaluates over 500 TBI cases/ year (<http://www.njneurosurgeons.com/neurotrauma--traumatic-brain-injury.html>). Moreover, there is a Neurosurgical ICU with 24/7 coverage by Neurological Surgery attendings

and residents and 24/7 coverage by Neurology attendings and residents for neurological and epilepsy monitoring by Video-EEG and ICU EEG monitoring.

Current interests among the Neurological Surgery faculty include: 1) Transcranial magnetic stimulation in patients with TBI; 2) Use of MR-Spectroscopy to predict the emergence from coma or the vegetative state following TBI; 3) The use of adjunct osmotic diuretics in the management of elevated intracranial pressure; 4) Investigations of decompressive hemicraniectomy in the management of severe TBI. However, no currently funded research protocols in these particular areas exist. The limited clinical research in these areas or any other acute and subacute interventions in either TBI or SCI is thus a major missed opportunity to establish a “best in class” research program to bolster the reputation of Rutgers, increase its research funding and serve the people of NJ. Clearly, increased interactions among the basic and clinical investigators will enhance the excellence of the program in Traumatic CNS Injury.

Although the two focal areas of Neurodegenerative Diseases and Traumatic CNS Injury are distinct, many different types of brain dysfunction and injury have common features that include cellular damage and inflammation. Traumatic CNS injury is the consequence of an initial trauma that impacts the brain or spinal cord, with common sequelae leading to continued neuronal damage and functional impairment. While MS and PD are not the result of an initial trauma, these conditions also result in cellular demise in the CNS. One common element of these conditions is the resulting neuroinflammation, which contributes to continued cell loss and functional impairment. The primary cells affected in MS are the oligodendrocytes, but white matter damage is also a common feature of Traumatic CNS Injury and PD. Similarly, whereas neurons are primarily the target of PD, neurons and axonal damage are features of Traumatic CNS injury as well as MS. Understanding the mechanisms of cellular demise, inflammation and pathology in these injuries and diseases will illuminate commonalities and differences that will enhance our understanding of the mechanisms governing cell loss in the brain, and will identify potential avenues to pursue to develop therapeutic interventions for translational and clinical studies.

Gaps

Although many strengths are readily apparent in the Neurodegenerative Disease and Traumatic CNS Injury Foci, gaps are also evident.

1. A critical mass of faculty at multiple locations is needed to enhance and extend collaborative research. While we are succeeding as individuals, faculty recruits that facilitate collaboration are critical at the basic science, clinical and translational levels. In particular, expertise lacking at our institution exist in the following areas:

- A. Basic scientists expert in neuroimmunology, as neuroinflammation contributes to the progressive neurodegeneration apparent in PD, MS and CNS Trauma.
- B. Investigators dedicated to exploring commonalities in glial and neuronal dysfunction associated with Neurodegenerative Diseases and Traumatic CNS Injury and who use state-of-the art animal models of disease to explore neuropathology.
- C. Basic or translational scientists expert in the genetics of these disorders. While there is very strong neuropsychiatric genetics at Rutgers, there is no expertise in the genetics of PD or MS.
- D. A nationally/internationally recognized expert at the Associate or full Professor level in Neurosurgery and/or Neurointensive Care who has a history of funded research to build a group to assess the acute pathophysiology and the treatment of acute and subacute TBI/SCI in our local patient population.
- E. Faculty trained in MS and PD clinical research; new faculty are necessary on each campus.
- F. An investigator with expertise in multiphoton microscopy and electron microscopy and an investigator with expertise in small animal imaging.
- G. Numbers of faculty in individual areas of investigation at each site are relatively low, limiting our ability to publish and receive numbers of grants noted at the top regional institutions and the Big Ten.

2. Critical state-of -the art- cores need expansion.

- A. The nervous system is difficult to study in living organisms but advances in imaging technologies, such as structural and functional MRI, have made these studies possible. To achieve “best in class” status imaging facilities need to be upgraded and available at both campus locations. For instance, PET/CT scanners and a high resolution MRI are needed for animal imaging on the Newark campus, while access to a 3T MRI for human studies is needed on the New Brunswick campus.

B. State-of-the-art imaging facilities that include multiphoton microscopy and a digital electron microscope core facility that includes ultrastructural immunocytochemical analysis must be expanded.

3. A lack of institutionally organized events to stimulate translational neuroscience research and enhance communication among the faculty. Significant barriers to collaborations between the many excellent basic scientists and clinician scientists on the greater Rutgers campus exist. Needed are:

A. State-of-the-art telecommunication facilities in multiple locations throughout Rutgers.

B. A pilot grant mechanism that funds collaborative projects materializing as a result of new interactions within the *Neural Injury and Repair* group.

C. Administrative support to facilitate the submission and administration of training grants, multi-investigator grants and individual grants.

D. IT support to develop a web site to service clinicians and scientists who will participate in this initiative.

4. A lack of a drug discovery core and mechanism to foster translational/clinical trials.

5. A lack of liaisons with biotech and the pharmaceutical industry.

Opportunities for Collaboration

We are strengthened by a number of opportunities to collaborate and extend our expertise.

1. Funding is available from the NJCBIR, NJCSCR, the NMSS, the NIH, the Michael J. Fox Foundation, the DOD and potentially the recently established funding partnership between the NIH and NFL to pursue basic and clinical research. Potential for an NIH Center grant application (Udall Centers of Excellence for PD) exists to support basic and clinical research. Collaborations between basic and clinical scientists will enhance opportunities to receive such resources and our ability to define commonalities and distinctions, in Neurodegenerative Diseases and Traumatic CNS Injury.

2. The Big Ten/ CIC Ivy League TBI Collaboration has been established. Rutgers faculty members have begun interactions with this group that is dedicated to bringing together clinicians, coaches, athletic trainers and academics to study the effects of head injuries in sports. This collaboration that began in 2013 includes a centralized data-sharing platform to share research related to TBI.

3. Plans are underway to consolidate the Neurological Surgery services at NJMS and RWJMS under the leadership of Dr. Charles Prestigiaco, Chair of Neurological Surgery at NJMS. This should facilitate coordination of clinical research projects at the two medical centers and support our abilities to excel in the understanding and treatment of Traumatic CNS Injury.

4. Rutgers is in position to lead a consortium of 5-7 MS centers in NJ to become sites for large-scale multi-center clinical trials.

5. Rutgers is in a position to collaborate with investigators associated with the Kessler Institute for Rehabilitation who are conducting basic and clinical research associated with Traumatic CNS Injury as well as MS. A number of these faculty have appointments with the PM&R Department at NJMS and already participate in collaborations and PhD training with RBHS faculty and programs.

6. Rutgers is in position to collaborate with investigators associated with the VA who are conducting basic and clinical research associated with Traumatic CNS injury. A number of these faculty have joint appointments with the Neurology Department at NJMS as well as collaborative projects with NJMS faculty.

7. Investigators from RBHS have served or serve on Study Sections of the DOD, NIH, American Parkinson's Disease Association (APDA), the Progressive Supranuclear palsy (PSP) organization, the NMSS, as well as the NJCSCR and the NJCBIR panels, putting our scientists in contact with those knowledgeable about directions of funding opportunities and in position to impact public policy regarding these diseases at the national level. This expertise needs to be mobilized.

8. Collaborations with EOHSI exist that can lead to grants studying environmental risks for PD and PSP.
9. The NJ Commission of Health recognized issues related to access to care and treatment and consequently appointed a task Force to address the unmet needs of MS patients in NJ. Rutgers MS Centers are in position to impact public policy regarding MS in the State of NJ. The Directors of the two Centers: Drs. Cook and Dhib-Jalbut serve on the State of NJ Task Force for MS and the NJMS Metro chapter Board of trustees respectively.
10. Opportunities exist for Rutgers neuroscientists to collaborate with Rutgers Biomedical Engineers engaged in tissue regeneration research, with Rutgers pharmacologists who can help us bring promising new drugs to PD, MS, SCI and TBI patients, with Rutgers clinician scientists to help us to translate basic science discoveries into new therapies and with Rutgers stem cell biologists to help us to promote CNS regeneration and repair.
11. Collaborations with Rutgers physical therapy program at SHRP that offers continuing education courses in PT management of concussion can be initiated.
12. Centers for basic research and clinical diagnosis and treatment of PD now exist at the RWJMS and NJMS campuses that provide opportunity for cross-campus collaborations.